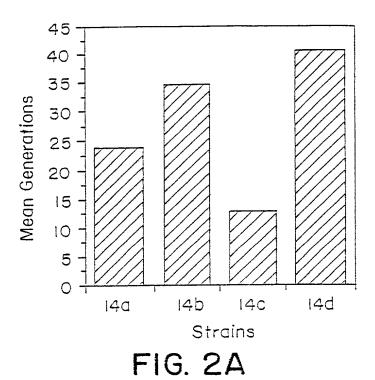
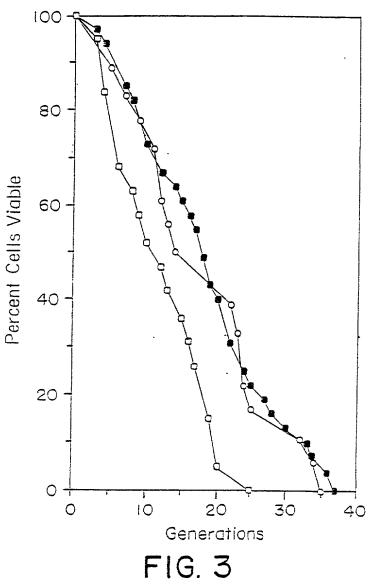


FIG. I



Strains

FIG. 2B



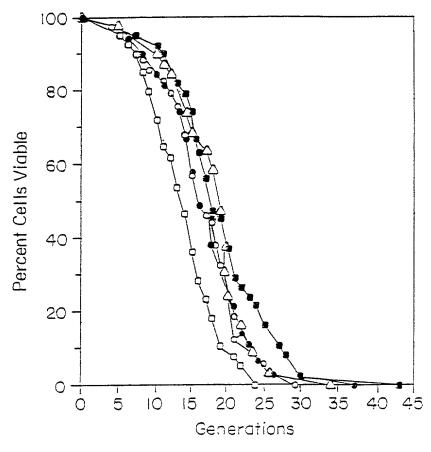


FIG. 4

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

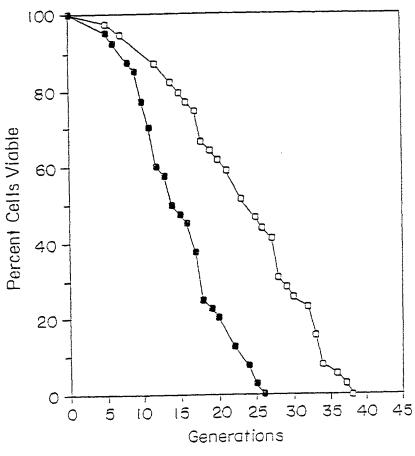


FIG. 5

÷ _

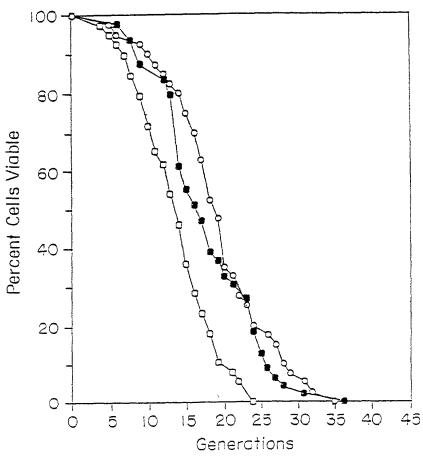


FIG. 6

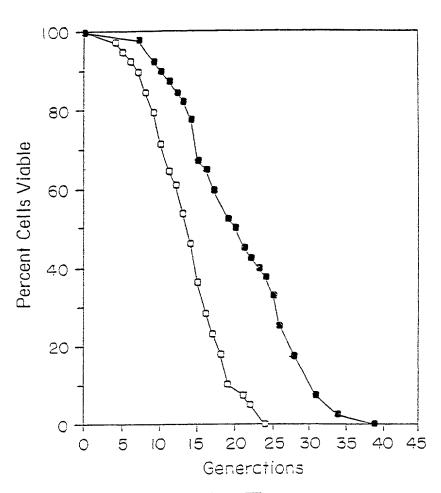


FIG. 7

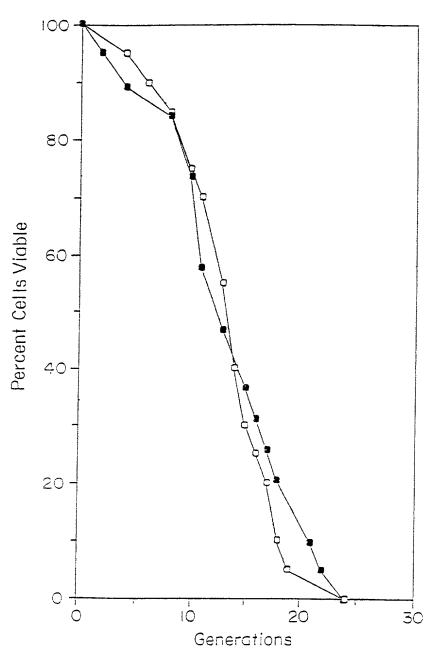


FIG. 8

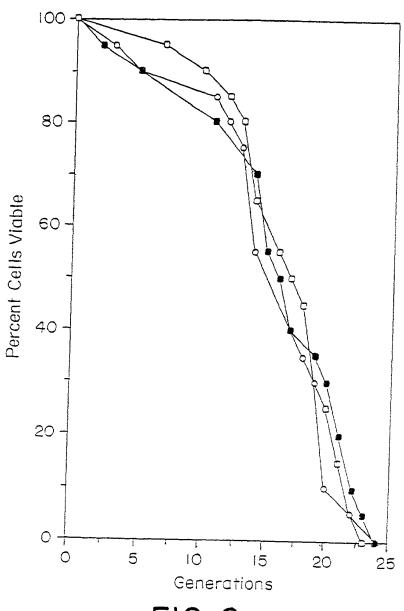


FIG. 9

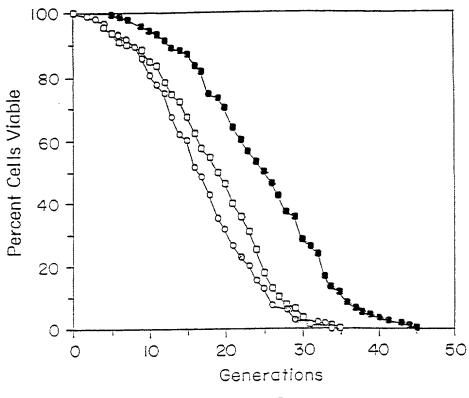


FIG. 10

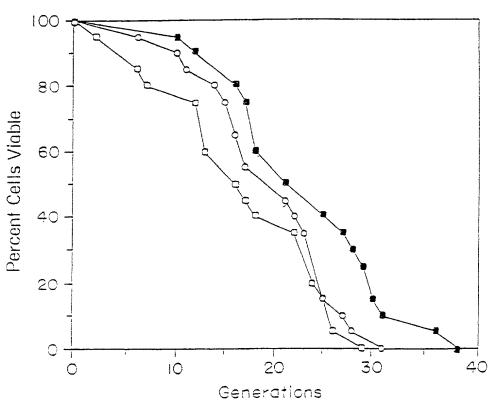


FIG. II

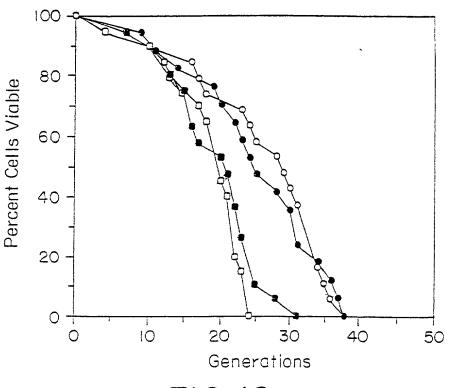


FIG. 12

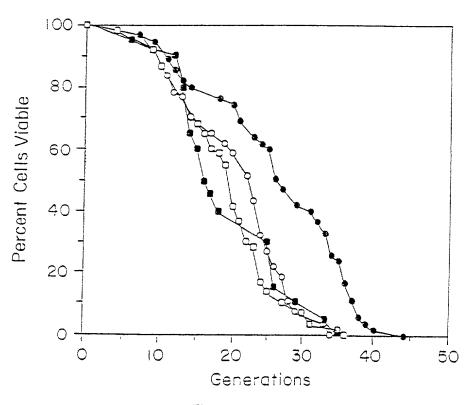
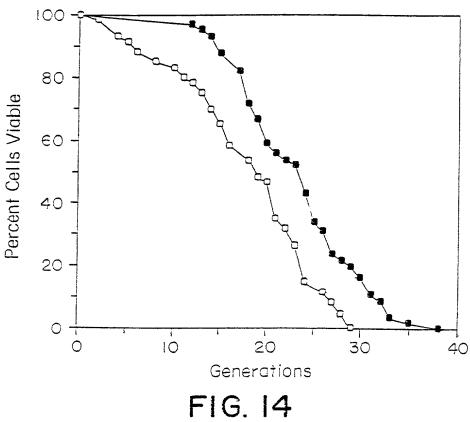


FIG. 13



Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

| 96 | 3 188 | 7 0 | 369 | 444 414 | 519 | 594 | 669 | 744 | 819 | 894 191 | 969 | 104 4 241 |
|---|--|-----|-----|--|----------------------|-----------------|---------------------------------------|----------------------------|---------------------|----------------------------|--|---|
| TGAAAAACTGGAACTAGACCCCACGTCAGGGGCCTTCA ATG TGT TAG AATACACAGGGGGCTAGTTCCTGGTGCCTGGATCTCGAGG 9 | GT CCA TAA AAAGAA ATG TAG AGGTGGTGTTGACGTTTTTGCCGC P * A A A A A A A A A A A A A A A A A A | | | GAT TTT AAA CCG CAA TTT ACG CTC CTT TCA TCG GTA ACT AAG AAA AAA AAA AAA GTA CGA CCA CAC AAT D F K P Q F T L L S S V T K K K K K K V R P H N | AAC CAA CTA N O L | TTA TCC GCT CTA | GAC AAC CAC CAC AAC GAC D N H H H N D | GCC ACC ACC GCT A T T A | TCG ACT GCC GCC GCC | TCT GTT GGT TCT S V G S | GGA GAT TTT GAA GAT GGT ACC ATT TCC TGT TTC CCA TCC GGA CAA GGT GCT GTC TCC TTG GAC TGG TTA 969 G D F K D G T I S C S D F P S G Q G A V S L D W L 216 | GGF CTA GGC GGC TGG GCT TCC ATC ATG GAC ATG AAC GGT AAC ACC ACC TCT TGT CAA GAC GGA TAC TAC TGT 1044 G L G G W A S I M D M N G N T A T S C Q D G Y Y C 241 |
| | 97 | 189 | 289 | 370 17 | 445 | 520 67 | 595 92 | 670 117 | 745 142 | 820 167 | 895 192 | 970 217 |

FIG. 15/

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

| 1119 | 1194 | 1269 | 1344 341 | 1419 | 1494 | 1569 | 1644 | 1734 | 451 1809 | 1894 | 1946 |
|------------------------------|----------------------|----------------------|----------------------|----------------------------|----------------------|----------------------|----------------------|----------------------|---|--|---|
| T AGA TCC GTT GGT R S V G | GAA GGT CAA | TCT GAA AAC S K N | TAC TAT CAA Y Y Q | TGT ATC C I | ATC ACT TAC | GAT GGC TCT | GTT TCA GTT | TTTTACTCGT | AGT CCT TTG TAC TAT CCC TTT TAT S P L Y V D R V | ATG | |
| CCT TCC GAT GGT P S D G | TTG TGT L C | TAT CCA Y P | GAG GAC K D | GTG GAA GAT GGT V K D G | GAT' D | GTT GCC V A | GGT TGT | CTTTTGCTAGTACT | GT CCT TTG TAC | ATATTATCATATAGCATATTATATAACATAAAAAGTCAAGAAAAAA | |
| GAA CAA K Q | ACT AAC T N | GGT ACC G T | GTC ATC V I | GTC TCT V S | GCT GGT A G | ATC AAG I K | GGC TCT G S | FTGCAAATAAG | A AAA CAC AO K H S | GCATATTATA' | TGA TTGC |
| TGG CCT TCT W P S | AAC ACC GAC N T D | GCT ATC A I | CCA ATC P I | AAC GCT GGT N A G | GTC TTG V I, | AAC N | TCT GGC S G | TCCTTGAATA1 | CAC AAT ACA AAA AAA CAC III N T K K H | TATCATATATA | T'IT T'IG CAT 'I'I'C GAA TGA I'I'GC F L II F B * |
| AAG ACC CAA K T Q | TAC CGT TCC Y R S | GGC TCC AFT G S 1 | TCC TCC CAA S S Q | TAC GTT AAC Y V N | GCC CCA GTT A P V | GAA GCA CÇA K A P | GGT GTC TAC G V Y | TAG GCCTTTTT | TTT TTC CAC F F H | CAC TAG ATAT H | CTT TTT TTG |
| TAC GCT Y A | TTA L | T'C'C S | | rac Y | ľGG √ | AAA K | AAT | rac ' | icg 3 | AGA TAC CA R Y H | TAT Y |
| CCA GGT P G | AAC GGT N G | AAC AAG N K | GTT GGC V G | TCT GCC S A | GTC GGT V G | CCA AAC P N | TCT TAC S Y | TTT GTC F V | TCA ATT S I | ΥΥΥ ΥΥΑ F L | ATA ACT 1 T |
| GCT TGT TCT A C S | TGT C | GCT A | CCT ACC GTA P T V | | TCC S | | | TCT GCT AAC S A N | GTT TAT TTT V Y F | ATT TTT TCT I F S | TCA CTT TCT S L S |
| T'AC Y | TTA L | GCT A | GTT V | 667 6 | GAG K | ATC 1 | GTC AAT C | 66T 6 | TTT ATG G M V | | ттт тта т Р L S |
| 1045 242 | 1.120 267 | 1195 | 317 | 342 | 1420 367 | 1495 392 | 1570 417 | 1645 442 | 1735 1 | 1810 25 | 1895 2 |

FIG. 15E

| | GGA G E N | | | TCT S L | TTT F F |
|---------------------------------------|----------------------------|----------------------------|-----------------------------------|---|----------------------------|
| CAG Q S V | TAT Y M W | GAA E K K | AGA R E K | ${\rm TAC} \\ {\rm Y} \\ {\rm T} \\ {\rm L}$ | CTC L S L |
| CTT L F | TCG S R | CTC L S R | AAA K K K K | TTT F F L | TTC F S P |
| CAG Q S A | ATG M C V | TTT F F S | AAA K K K | GGA G D I | GTC V S L |
| AAC N T P | TTT F L Y | GAT D I F | AAA K K K | raa * K R | rrr L C |
| AAA K K K | CCG P R V | AAG K R R G | AAA K K K K | $\begin{array}{c} \text{TTA} \\ \text{L} \\ \text{Y} \\ \text{I} \end{array}$ | TGT C V |
| ACC T P Q | TCT S L S | TAT Y I | AAA K K K | GAG E S V | rtg L C V |
| | CAA O N I | | | | |
| | TAA * N N T | | | | |
| 31/1 AGC S A H | 91/3 GTC V S S | GAA GAA E N N | AAA AAA K K N N | ATT ATT I F | 331/ GCA A H I |
| AAT N I | GCG A R G | CTC L S R | CAA O K K | CAG Q R D | CAA Q K S |
| ACA 1' Q K | TTA L * | T'I'T F F S | AGG R G A | ATG M C A | AAT N I S |
| ACA T O N | 717'F F F | TTA L, Y I | CTC L S Q | T'I'I' F L Y | TAA * K K |
| CTA L * | CCT P L | ACC T P L | CGC R A P | AAA K N I | TTC F S L |
| CTT J. F. S | ACG T R | CCT P L | AGG R G A | GAA E K K | TCA S H I |
| GAT D 1 S | GAC D T' H | GAC D T P | | TAT Y M | |
| CGG R G G | ATC I S R | CTT L L L | GGA G E K | ATC I S L | TAG * R G |
| TAA * N T | CCT P L Y | A'FA I Y T | TCG S R G | AAG K R D | ITA L Y I |
| J / I AAG CTT K L S F A L | CAG O S S A | TCT S L L Y | GCT A I, F | TCG S R R E | TGG W G |
| J / L AAG K S S A A | GAT D I S 121/ | ATT I F F 181/ | AGG R R G G G 241/ | GAT' GD I F 301/ | T'T'A L Y M |

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al.

Inventors:

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

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Title: Genes Determining Cellular Senescence...

Leonard P. Guarente, et al.

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| TTG L C V | AAA K K K | AGT S V | ATA I Y I | $\mathbf{TAT} \\ \mathbf{Y} \\ \mathbf{M} \\ \mathbf{C}$ | TAT Y I | CAG Q S |
|--|--|------------------------------------|----------------------|--|-----------------------------------|---|
| CTA L Y I | TAC Y T Q | TGC C A A | TAG * R D | AAT N I L | AAT N I L | CTG L C A |
| ATG M C A | TAC Y T L | T'FG L C V | TGT C V | ATG M * | AAA K K K | GGA G D T |
| TAG * R D | GCG A R | AAA K N I | TTC F S L | CCA P O N | TTA L * | AAA K K K |
| TCA S H II | GTT V L | TGA * E K | AAT N I | ${\rm TAT} \\ {\rm Y} \\ {\rm I} \\ {\rm S}$ | TCA S H I | ر ال من من |
| TCA S H I | GTT V L | CTG L C | TCC S P Q | $_{\rm F}^{\rm GTT}$ | AAT N I | CCT P L L |
| | | | | | AAA K K K | |
| TTG L W G | AAC N T H | AAA K N I | ATA I Y I | TTA L * N | TGG W G | 6 6 6 6 6 |
| /55.7 AAT N I F | ATA I * I | TCA TCA S O K | ATT I L Y | /631 TAT Y I | 7,651 1"FG L, C | A'tG A'tG M W G |
| 1651 CAA Q K K | CCC P P H | 1 / / 1 TTT F F F F | GTA GTA V V | 1891 AGT S V L | 1951 ATG M C C | ACA T D D |
| CAT' II I S | CTA L Y T | AAA K N I | TCG S R G | CTG L * E | CAA O K K | ATA 1 * N |
| CGC R A P | 'l''I'T F F S | AAC N T Q | AGT S V | TGG W G | CCT O L S | TTA L * |
| TCT S L S | CCA P H I | TAC Y T Q | ATC I S | $\mathbf{rar}_{\mathbf{Y}}^{\mathbf{Y}}$ | TCT S L S | T'TG L C |
| AAT N I F | ${\rm TTA}_{\rm L} \\ {\rm Y}_{\rm T}$ | CTC L S L | ACG T R D | ACT T L L | AGT S V F | TTA I. Y |
| TCA S Q K | T'CA S II I | GTA V Y T | TCA S O | TTT F L L | TGA * E K | $\begin{array}{c} {\rm GAT} \\ {\rm D} \\ {\rm I} \\ {\rm F} \end{array}$ |
| 4 4 4 5 | ATA 1 Y I | TTT F L C | TAA * N I | ACT T L | GTT V F | CTG L W G |
| GTPA V Y I | ATA I * N | GCG A R | GAT D I L | TGG W G | CTT L L C | TTA L Y T |
| AGT S V C C | AAA K K N | TAA * K S | CTG L M G | AAT N I I | TAT Y I | TCA S II |
| 1/54 AAA K K K K 1/563 | AAC N T T O | TAC Y T T I, | F F S P | AAG K K R E | AAC AAC N T T L | GAA GAA E |
| 1621/541 TTC AAA AGT GTA F K S V S K V Y Q K C I 1681/561 | TAG * R R E | AAT N T T L 1801 | TCC S P P | LBB TCA S Q K | 527 GTC V S S 1981 | TPTA TI * |

Docket No.: 0050.1491-005
Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

TGA ACA ITIC TITI TGA CTA CCA TTG ATA TAT GGC AAA ACA GCT CTA GTA CAT TGA ATT ACG GTA ACT ITT GTA ACG ATT TTT CAT TGA AAA TTG TCC TTA CAA AAG AAT TAC TTC CAA GTA TTA AAA CTA CAT CCT ATG CAA AGA AAA TTA AGT TGA AAG TTA AAG CTT ATG CAG AAG CCA CAG GTA TAC CAT TCA CTG ACA TAT CTC CTC AAG TCA CTG CAA TGA GTC ATA ACA ATC TTC AAA CGA TTA ACA ACG AAA TIG CIT CIG AIG ACG TGA ITA AIG CITI CIA 2221/741 2341/781

FIG. 161

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente, et al. Inventors:

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|----------|---|------------------|------------|----------------|----------|-------------------------------------|-------------|------------|--|----------|---|----------|----------|----------|------|---|-----------|------------|----------|----------|---------|----------|---|----------|----------|-------|------------|----------|------------|--------|------------|----------------|----------|----------------------|
| | 4 | ₹ ≥ | : ` | , ,_ | | 70 | | ט ג | | | ' AT | Ξ | 0 | | | A | — | Ø | | | NG. | Ħ | ; | | | CI | Ч | ೮ | | | ဗ္ဗ | ೮ | O | |
| | ACC | ; = | , <u>p</u> | 4 | i | TAC | > | , E | , <u>p</u> | 4 | AAT | N | H | × | | CAT | H | H | X | l | ATA | H | * | Z | | CTG | 1 | ບ | Ø | | CAA | a | × | × |
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| | ATK | <u> </u> | ָני: |) = | : | Tru | Ę. | , <u>F</u> | 4 | 2 | CAA | ø | × | Z | | AAA | × | × | Z | | TAA | * | × | Ŋ | | CTA | П | * | Z | | ATG | Σ | ပ | > |
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| | ည | Ъ | Д | H | | TA I | _ | * | z | | CC A | H | വ | = | | GA A | ¥ | <u>6-3</u> | × | | ng C | ≖ | מז | Ø | | E I | Ω | . 7 | Έı | | II C | × | F. | ಬ |
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| 821 | BA A | : | Ħ | z | 941 | ZA A | H | ~ | z | 361 | IG C. | , | | W. | 381 | CAC AAG ATC AGA AAA TTC A | Η | پ پ | _ | 01 | N IK | 3 | | . | 7.1 | C AA | × | × | ď | 41 | A TC | ຜູ້ | <u> </u> | H |
| 2461/82 | l'A A | × | ~ | × | 2521/841 | ₩ 13 | Ţ | × × | = | 2581/861 | JA A'I | Ξ | ب ب : | z | 41/6 | KC AZ | × | , T., | o. o≃ | 2701/901 | T CG | æ | _ : | χ. Σ | 76/10/7 | T TA | X | ₽, | _ | 21/9 | V C ນ | œ [?] | z | Ъ |
| 24 | Z | | • | | 25 | ົວ | - | U2 | | 25 | J. | <u>،</u> | * | , | 76 | S | = | Ħ | | 27 | ၁ | 24 | , | | 17 | 5 | ~ | > | | 28 | X U | = ; | ₽ | _ |

GNT TTA AGC AGC CTG GAT TTA TGA 1GA ATG AAA CCG ACA AAA TTA ATG CTA ATC ACT TCT

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente, et al.

ATC AAA CGG AAG GTG CAA ACT GGG ATT CAA GTT TGT CAA TGA AGT CGC AGC ATA 1TG GTC TGA ATA CCG CTA GAA CAT CTG ATG AAC TTC AAT TCA CTT TGC CAT AAT ACT TTT TTT TCT AAT AAA AAA TAA AAA ATA AAA AAT TCA ACT AAG CAA TGA CGT CCT ACT AAA GTC CCA AAA THE THE THE THE CET THE TAC THE ACA AAT ATT THA CHE AGA AAT CAA AGA CAA AAG 3091/1031 3121/1041

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Title: Genes Determining Cellular Senescence... Inventors:

Leonard P. Guarente, et al.

THE GAA CAE GTA THE AAA ATE CITE CEA CITG CET TITG CAG GET TAG CAT TEC THE CITA CEA ITT GAG CCG GAA AAA AAT GGT AAA GCA AAC TAT TGC CAT CIT TAT AIT ITG TAT TCT GTT 3331/1111 TIT TIG AAT CGT TIT TIG IC F L N R F L 3421/1141
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M I * F 3361/1121

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al. Inventors:

241/81 TAA TGA TCA ATA TAG TAG GTA TAG TTA TAT TCT TAT TCG TTG CAC CTT GTT TAA CAA ATC ACT CAG ACT CAA AGA GAA TAT CGG TTG GTT ATC TCT CTC CGA AGG TGA ACA GCA AACI I T Q T Q R E Y R L V I S L R R * T A N S L R L K E N I G W L S L S E G E Q Q T GAA TTA TAT CTG TCC AAT ACC GIT GCC TTG THE THE TEG GET CET CEA GAG AAT AAA AAA CTT TGT GAC TGC AAA TTT TAA TTT GTG ACG CCT TTT CTT ATT ACT CAT GTA TTT GTC ACT GTG TCT TCC ATG GAG TGA ATT GTG ATT TGT CTT GAC GAT TGT TTT TTT TCT ATA TTT TTT 181/61

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al*.

CTT CCG TAT ATT ACA TTG TAC ATT ATT TTT ATT GTA TTT TAG TTT CCA ACG TTA GGA TTT TCC AGA CGA TTT ATT TTT AGT ACA TGA AAG AAG AAA TCG ATG ATG TAC CAT CAG TAG ACC CTG TCG TAT CTT TTA AGA AAG AGA GAA CTA AGC GCT GTA ACA TTT TTA AGT GGA CCT ACG 691/231 601/201 CTT TAG GTT CTT TTA AGA GTC TCT GTT CAT GAG CCG TCA TTA ATA CTA CAA AAG GTT 661/221

FIG. 171

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

AAA CAG TCA ATT CTG CTT TAG AGC AGT TGC AAC TAG ATG ATC CAG AGG AAA ACG CCA CCT TAA ATG ACA ATT CAA TGA AGG TAT TGC CAA TCG CAT GGG CTG ATC CGT TITT TITC CGC CCC CTG ATT TTA ATG ATC CAA CAC CAT TGA GTA GCT CGC CCT TGA ATG CAG GCG GTC CAC CAA TGT TAT TCA AGA ATG TGT CTT CGG GTG CTG CGG TAG CAA CTC AAG GTG GAC AAA CTC AAG ATT CTC AAT 991/331 TGC AGG TITC CITC ATA ATC CITT GIC CAT CTA ATG CAT TYG CGA ATA AAG TYT AAA TGT TTC CAC ATC CAC AAA 901/301 1021/34 961/321

wia.

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente, et al.

tat gga ctc att caa acg tac cag gat cag cat ctg tag cca itg aag aaa cca ccg cta cct igt caa agg act icc aat ctg aca igc aga att itt cta agg cta aga aac cgt ctg CTA AGG GCA GGG AGT CTA ATA ATA AGG CTA GTT CGT TCA ATG CGG CCA ACA ATG GTG TIT CIG AGA AAT TAT CCG ATT TTA ATA AAA CTG CAC CAG CTA AAA AAG AGA GAA CTC AAT CCA 1411/471 1351/45] 1471/491 TTC ATG CTT TAT CAC TAG GAG CTA ACA ATA CTG CAA AAA CCA I'NG NAA CCT CGA AGG AGG ATT CCT CAA CGT CAT U GAA GAC AAA 1321/441 1381/461 1441/481 1501/501

Title: Genes Determining Cellular Senescence... Inventors:

Leonard P. Guarente, et al.

GAC CITY TAC TITC AAC CAA AIC CITA TITA TGC TIT CAG ATA TGA AGA ATG ATG GTG GTA AGC CCA cca ccg ata acg aca agg cgg gtc caa atg tta gga 1gg att taa taa atc cta atc ttg TAA CCC AAT CGC CAA TTC ATC TTG CAC CTT ATG AAA TGG GGG CGC AAT TTC AAC CTT TCT CTC CGA TTT TAA ATC 1831/611 CAA CTT ATG GTG CAG CAT ATC CAT ATG GGG CAG GCC ACC CAC ATA ATA TAT CCT CCC CTA CAC TAA ATG CAA ATT CTC CAA TTC CTC CAA ATT CTG TTG CCT 1861/621 1921/641

GGC CAT CAA TGC AAC CTT TCC ACA TAT TAC CTC CCC AGC AAA ACA CCC CCC CTC 1981/661

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

GGC TIT ATA GCA CITC CAC CTC CCT ICA ACG CAA IGG TIC CGC CIC AIT IGT IGG CIC AAA GTA AIT CTA ATT ACA ACA ATA AAG ACA CAG TGA AAA ACA GTT ATC ATG GCT ACT ATA ATA GTA ATG CTA CCA ACA GCA acc ant ata icg gaa gta tic act cat igt gta aag acc aac aig git gic git tic igc ACA GCG CGG AAA AAC AAC GTA AAA TIG AGG AGT CGT CGA GAT TIG CGG ACG CAG TYT TAA TGA ATA GCG CCA ATA TGT CAA GTC ATA ATG ACA ATG ACA ACA TTG GTA AAA TGA AAA ATA ~ GIC GIT CIA ACG 2221/741 2281/761 2341/781 2401/801

2461/821

AAA AGC AGT TGG ATA TTC TCG GCA GTA AGG CGG CGG ACC GAA TTT TTG AAG AAA CTA AGG

K S S W I F S A V R R T E F L K K L R

K A V G Y S R Q * G G P N F * R N * G

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al. Inventors:

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| 4 | 17.7 | § * | <u> </u> | Η. | | CTT | 7 | <u>Se</u> 4 | ຜ | 2671/891 | TCA | co | = | Η | | ATA | H | × | Ŧ | | GGT | Ö | > | ï | | TTG | | Y * Y C | ¥ | |
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| | T Artur | H | H | × | _ | AAA | × | Z | H | | AAA | ¥ | × | × | _ | CCC | ¥ | գ | Щ | _ | 1330 | ಬ | × | ¢ | = | TTG | П | * | Q | 1 G |
| A . D | 47 KB / T | 4 V | * | Z | 1/87 | CAA | œ | × | × | 1/89 | TAC | × | H | Ċ | 2731/911 | TAC | ¥ | E | × | 2791/931 | GTT | > | Ē. | 7 | 1/95 | GTA | > | × | H | FIG. 17G |
| 4 1 | C C Z | S S | £ | Ö | 261 | TCA | 23 | Ħ | H | 267 | CAT | Ħ | H | I | 273 | CTT | ч | <u> </u> | 1 | 279 | AAT | Z | E | ೮ | 285 | GCT | | . 3 | • | 正 |
| € | THE C | 1 = 1 | H | ĵz. | | TAC | 7 | H | <u>,,,</u> | | 999 | IJ | O | × | | ATT | | ă. | ល | | AAA | × | × | × | | ATA | H | * | ر در | |
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| כ | 200 | \$ * | 0 | Ţ | | AAA | × | × | × | | ATG | X | Ø | O | | TTG | П | ပ | > | | ATG | Σ | ೮ | > | | CAA | | z | ; | |
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| | 1 725 | § 2 ≃ | ೮ | > | _ | TTA | J | > | H | _ | CCT | ρı | ᆸ | ı | | AAG | × | ~ | H | | TAA | * | × | Z | 7 | TTA | 7 | X | H | |
| : د د | 2521/841 Amp Ama | I I R L N | X | 1 | 2581/861 | AGG | ~ | Ö | > | 2641/881 | AAA TIT CCT TAA ACC CIC | <u>Bu</u> | ᅜ | I S L N P | 1/90 | ATG | Q M K K II R L L L I | * | FI | 1/92 | A'I'I' | H | Ĭz., | Ţ | 1/94 | AGT | S | > | | |
| 4 (| 797 amm | I | ľ | X | 258 | AAG | × | ĸ | 떮 | 264 | AAA | × | z | Τ | 270 | CNG | ŏ | ~ | | 276 | NGG | × | ŋ | _ | 282 | TCC | S | 24 | ø | |

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

AGA CAG CAT TAG ACA TTT CTC ATA AGC AAA ATG ACT ATC TCT ATA AAA GAC TAT CAG AGA THA CCA AAG AGG CTG AGA AGA ACA AAT ATG ATT ATA CGC ATA AAA TTG TTG GAT CAA ATG TGA GGT GTT GCG TTT TGC AAC GTT GTC TAG ATC ATG GGA CTA CAG AAC AAT GTG ACA ATC TGT GCT ACG GAA ATT ACG TTT TIG GCA ACT ATG CAT TCC ACC TGT TGA AAC CAA GAG CCA TCG AAC TTT CTA TCC ATA AAT THE AAA AAA TET TEA AGA CAG ETA TTG TTT CGG AGE CAA TGA TIG TIG ATA AAT TAA CIT TGG ATC TGA ATG ATA 3091/1031 3151/1051 ATG GTG GCG AGA CGG GTA TTC AAT CAT TGT GIG ATA AGT IGC TAG CCC I'GC AAT ATA TAA 3121/1041 3181/1061 3061/1021 3001/1001

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

TAN ACG TCG CTC CAC AGG ATA CTG TAG AGG TCC TCA AGA TTT ATC TAT ACA AAC AGT GTT GAA GAA ATA AGA GAA GGA GAT CGC CCT AGA AAA CAG AAT GTT CTT ATT TAA ATA TAT GGT ATA CTG GTA AAT THT THE THE CGF TGA GGA GAA ATA CAC CTC ATG GTA AAA GAA TCA TCG TIT TAC GIT AGT AAA CTC AAA AGA AAA AAA GGA AGG AAG TTT 1TG AGA ACT TAC AAT ACT AAA ATA CAT CAT TCA AAT GAA TAT CCA AAG CAA AAA AAA TAG GAA TTT TCA CTT 3691/123] 3511/1171 3331/1111 THE THE CHE CTT TAC THE THE GCC CCA TAA CAT AGT TCT GGA CT'T T'IG CTA GTA TAC GTT TAA GAA TGT TAC 3601/1201 3661/1221 3481/1161 3541/1181 3301/1101 3361/112]

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente, et al.

| 3/21/1241 | 4.1 | | | | | | | | 3751 | 3751/1251 | - | | | | | | | |
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| > | > | > | > | Z | j - i | > | Z | H | > | Ē | H | > | > | > | > | 0 | <u>[z.</u> | H |
| 1/128 | 31 | | | | | | | | 3871 | /129 | ,, | | | | | | ı | i |
| GTG | TTC | ATA | AAT | TIT GIG TIC ATA AAT GGF AC | ACT | TCT | P ACT TGT ACT GAA G | GAA | AA GTG GGT ATT 1'GC 1'GC TGA GCA 1'TG AI'T GG | GGT | ATT | TGC | TGC | TGA | GCA | TTG | ATT | TIG AIT GGT |
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| TTA | GAT | TGG | ACT | 1GC | GAA TTA 1 | TTA | TIT TGC | TGC | CCA | TTT | GTT | GGT | TGC | CCG | TAA | TCG | GGA | Tric |
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| ATA | TCA | GAC | ACG | GAT | AAT | GAC | CTA | AAT | GAA | 25 | AAT | E | | | | | | |
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Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

Service Domard F. Guardino, Dr.

ace tto atg, cag aac atc agg ate ttg cag etg gga ete act gaa gat egg ggg get gaa ate eat ett eat eet ace get eeg eee gtg ttg gtg gaa tga gag ttg cag gcc gtt ccc agg acg acg cta tgg atg ttg ttt tga cat atg ggg ctg gga age age ttg 331/111cta cay ggt cyc aag cyc agc cac aac cag ctg gca aac atc gat ggc act act tot tto aga ggo ago atg gtg cca gac atg tea cag gat tga aac ato acc 301/101 241/81

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

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| | atg | Σ | * | Ω | | aaa | × | × | × | | atc | i | ಭ | Ö | | tga | ນ | Ø | œ | | CAC | = | H | ~ | | cgg | ~ | ဗ | Ü |
| | atc | H | ß | = | | gta | > | * | × | | gtg | > | * | Ω | | tgg | 3 | Ü | > | | aaa | ဌ | Д | C4 | | CCC | a | <u>a</u> | Ь |
| | tga | * | E | z | | cag | ø | x | ŋ | | tgg | 3 | U | Ö | | tca | အ | = | Σ | | tgt | ၁ | > | ß | | cat | = | | ß |
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FIG. 18E

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| 01/301 | | | | | | | | | 931/ | 311 | | | | | | | | |
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| 021/34 | | | | | | | | | 1051 | /351 | | l | | | | | | |
| tag ccc a | agc | tga | CCB | cca gca | CCA | atg | gtg | CCA | agc | ctg | tgg | agg | att | tot | CCB | aca | tgg | agt |
| а | ಬ | * | ч | A | o, | Σ | > | ч | Ø | ī | 3 | , H | — | ß | д | Ŧ | · × | מי |
| S P | K | Ω | œ | = | a | × | დ ე | a | æ | ບ | ಶ | ບ | Ē | 1 | Ö | = | v | > |
| Ö V | T | H | ಭ | Ħ | Z | ŋ | 4 | × | Д | > | Ħ | Ω | 红 | Ø | Z | Σ | Ħ | Ø |
| 1081/361 | - - | | | | | | | | 1111 | /371 | | | | | | | | |
| cc aga | gtg | tac | cct | tgg | acc | cca | tgg | aac | atg | tgg | gca | tgg | aga | cta | tto | agt | ttg | att |
| ~ | > | Ω | 4 | 3 | H | P. | 3 | z | X | · | æ | * | ಬ | Ţ | يعز | ູໝ | ı | H |
| P E | ပ | ď | Ţ | ŋ | Ъ | ≖ | Ü | T | ນ | ಅ | Ħ | Ü | ¥ | ಭ | ß | > | * | 1 |
| S Ö | > | Д | IJ | Ω | đ | Σ | Ħ | = | > | Ü | Σ | দ্র | д | 7 | ø | ĵz, | Ω | > |
| 1141/381 | | | | | | | | | 1171/391 | /391 | | | | | | | | |
| tt cag | gca | cda | agg | tac | ctg | tgg | act | cag | cag | cag | caa | ctg | tgg | gaq | ttt | ttg | act | aca |
| œ i | Q A R | ~ | × | Y L | T | 3 | H | | Q Q Q L W D F L T T | a a | т о | I. | × | Ω | Œ, | 1 | Ħ | H |
| F. | = | æ | ರ | E 4 | ບ | ಲ | 1 | | ß | ಬ | z | ບ | Ö | H | ţ٦ | * | ı | œ |
| S G | H | œ | > | 더 | > | <u> </u> | ಭ | -4 | ¥ | ¥ | H | > | Ö | Ţ | 124 | Ω | X | Z |
| | | | | | | | | | | | | | | | | | | |

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

cty cay can cta att cay cta atc aac aga cca ccc cac agg ctc agc aag gac agc agc L Q Q L I O L I N R P P H R L S K D S S gag tta ctc cct ggg gag tct acc ctg cca gtc ttt tcc agc agc aag ctg ccg ctg ccg cag ctg gat tgg ctg cag cag cga cac tag gcc cag ctg tgg tcc ctc acc agt att atg cty cgt tty toc cca atc cat aca tca tca gcy cty ctc ccc cay gga cgy acc cct aca ctg etc atc agc egc aca teg gtt tag etc eeg att cic aac aac agc igt icc aaa gac cia aig cgc iig cig icc agc agt iga cag cig agg tto tco gtg gag gag cca gcc aac gto ett tga ccc caa acc aga acc ago agg 1351/451 1411/47 Ö ctc agc agc agt atg 1321/441 1381/461

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al*.

cag tga att ctg ccc ttg cat ttg gac aag cca gtt ctt tct acg gca aca act ctc tga aca gca att cac aga gca gct ccc tct tct P V L S T A T T L * T A I H R A' A P S S tag ctc ctg ccc cag tca tca tta gtt cct cag ctg cac aag cag ctg ttg cag cag * * L $^{\rm L}$ P O L H K O L L O O ott tag gaa cac agc ctc agc ccc agc agc agc cca ata aca acc tgg L * E H S S L S P S P S S P I T T W gto ttg ctg gaa 1951/651 1891/631 ato coc ttg tgg cag otg cag ott L L r agc aaa cgg 1861/621 1801/601 1921/641

| 2041/681 | | | | | | | | | 2071/691 | /691 | - | | | | | | | |
|---|----------|----------|----------|------------|-----------|----------------|----------|----------|----------|----------|----------|--------|----------------|----------|----------|----------|----------|---|
| ccc agg got ctg ccc agc ctg cca aca cat cct tgg gat tcg gaa gta gca gtt ctc tcg P R A I, P S I, P T H P W D S E V A V I, S | gct A | ctg L | ccc P | agc S | ctg I, | cca P | aca T | cat | cat | tgg W | gat D | tog | даа Е | gta V | gca A | gtt V | ctc L | at cot tyg gat tog gaa gta gca gtt oto tog P W D S E V A V L S |
| D d | ľ | ບ | Ъ | Ø | ບ | C ² | Ħ | H | 1 | Ö | Ħ | 2 | × | * | œ | Ξų | ß | ~ |
| _ე | Ω | * | Q | д | K | Z | = | ß | П | ರ | æ | 9 | ß | ໝ | ಬಿ | Ø | 'n | Ö |
| 2101/70 | | | | ٠ | | | | | 2131 | /711 | | | • | | | | | |
| gog cca | CCC | tad | gat | ccd | CCC | tta | qaq | qqt | tta | ศลล | cad | cad | ttq | caa | act | cca | aca | ctq |
| A P | Ъ | , , | ם י | , H | Ъ | , ,,, | · 妇 | ; | , | · FE | , Ç | , a | , J | ø | ī | Q, | E | I |
| R | д | Ö | H | × | ď | 3 | × | > | X | z | ß | ಭ | ນ | × | .7 | ď | = | M |
| A T | 'n | IJ | ß | K | П | ೮ | ರ | Ē | ೮ | Ħ | .≪ | > | 4 | z | ಭ | Z | H | Ö |
| 2161/72] | _ | | | | | | | | 2191 | /731 | | | | | | | | |
| gca gtg | gct | acc | gca | gtg | act | CCC | tga | ctg | gca | gca | gtg | acc | ttt | ata | aga | gga | cat | cga |
| A V | Ø | ы | Ø | > | H | đ | * | ū | × | A | > | H | ĮŦ1 | H | R | 9 | = | × |
| M | 1 | а | ы | * | 1 | Дţ | Ω | × | œ | ø | * | ᅄ | ц | * | B | Q | Ħ | 田 |
| SG | Œ | ~ | × | Ω | ಬ | П | E | Ö | ß | ß | a | J | × | × | × | Ħ | ß | ß |
| 2221/741 | | | | | | | | | 2251 | /751 | | | | | | | | |
| gca gct | tga | aca | CCA | ttg | gac | aca | gtt | ttt | ata | acg | gaa | tta | gat | ttt | cct | act | cto | ctg |
| AA | * | <u>c</u> | д | , , | Q | ÷ | > | تح | H | F | ¥ | .T | K | يتز | 4 | д | J | ı. |
| O L | Ω | а | = | M | £-4 | ŏ | بتز | Ţ | * | × | ď | * | П | ĬΞij | ᄀ | ı | ಭ | X |
| S | Ħ | а | H | ŋ | ≖ | Ø | <u> </u> | × | Z | ೮ | H | ß | نحز | ß | ß | ß | ద | Ü |
| 2281/761 | | | | | | | | | 2311 | 1771 | | | | | | | | |
| gac ccg | tgg | gca | tgc | cto | tcc | cta | gta | agg | gad | cag | gac | att | CAC | aga | CAC | Cac | ata | att |
| D P | 3 | æ | ບ | L | ಬ | ľ | > | * | ۵ | ď | Ω | Ħ | = | R | = | = | ı | 7 |
| T R | ೮ | = | Æ | ಭ | а | * | ß | ŋ | H | x | ī | 늄 | E | ۵ | H | H | ಚ | Ŀ |
| δ | හ | E | വ | Ţ | ᅀ | Ω | œ | ಅ | Ъ | ా | = | ß | O ² | H | P4 | a | O. | ಬ |
| 2341/781 | | | | | | | | | 2371 | /791 | | | | | | | | |
| ace tet | ctt | cac | atg | gat | cct | ctt | caa | gat | taa | acc | tgg | gag | gac | tca | cga | atg | gca | gtg |
| PS | ľ | = | X | Ω | ᅀ | ľ | œ | Æ | * | H | 3 | 田 | Ω | ಭ | ~ | Σ | 4 | > |
| n a | ₽ | Ħ | × | - | Ţ | 红 | × | 1 | × | д | Ö | × | H | = | 된 | 3 | ø | 3 |
| I. S | ß | Ħ | Ü | ß | ຜ | ໝ | ß | 11 | Z | 7 | Ö | ŋ | Ţ | H | Z | Ü | Ω | Ü |
| 2401/801 | _ | | | | | | | | 2431 | /811 | | | | | | | | |
| gaa gat | aca | tct | ctg | ctg | ctc | cag | gcg | ctg | aag | ಭರಣ | agt | acc | gca | gtg | caa | gca | gcg | cct |
| E D | 1 | ß | 1 | | ľ | Ö | A | ľ | ¥ | Ъ | ន | ī | K | | ď | ¥ | ⋖ | r L |
| K I | = | Ţ | ບ | ບ | ಬ | × | ~ | * | ಬ | Ö | > | а | ø | ၁ | × | ø | × | 1 |
| RY | H | ಬ | 4 | æ | ᅀ | ೮ | K | 妇 | Ø | × | > | × | ಬ | < | ល | ß | 4 | Ø |
| | | | | | | | | | | | | | | | | | | |

| 2461/821 2491/831 | 1/82 | _ | | | | | | | | 2491 | /831 | | | | | | | | |
|-------------------|----------|-------------|-----|-----|----------|----------|-------------|-----|------------------|-------------|----------|-----|----------|------------|------|----------|----------|--------------|------------|
| CCA | dcc | tct | tca | dca | cga | gca | gca | cta | ttt | tot | ctt | cct | ata | gtt | tgc | gat | atg | gaa | tgt |
| ď | ¥ | ಬ | ន | Ø | ~ | 4 | A | 1 | Į r i | ಬ | 1 | ц | 1 | ^ | ၁ | Q | × | × | ນ |
| œ | Ω, | 7 | œ | ы | 퍼 | ø | = | Ω | × | ч | ţĦ | 'n | ಬ | ĮΣų | K | H | 3 | z | > |
| ಬ | 7 | Œ | ಬ | C4 | ß | ಬ | H | ч | 压 | ß | ಬ | Ω | α; | 1 | × | × | Ü | Σ | 22 |
| 252] | 1/84 | | | | | | | | | 2551 | /851 | | | | | | | | |
| ctg | atg | tca | tga | ott | ctg | gca | gga | gca | gga | ttt | tgg | aag | att | tto | gaa | aca | acc | ggt | acc |
| ľ | E | ಬ | ່ວ | д | ī | 4 | ဗ | 4 | | <u>F4</u> | M | × | H | ř. | · EI | E+ | H | ဗ | Ŧ |
| * | ပ | = | K | څې | 3 | ø | ы | œ | 4 | <u>5-,</u> | Ö | 2 | ĵz. | ß | × | œ | Q. | > | Д |
| O | > | X | а | ß | Ü | ~ | Ω | × | J | 1 | Ħ | Ω | ٠ ټد | ~ | Z | Z | ~ | × | പ |
| 2581 | 1/86] | _ | | | | | | | | 2611 | /871 | | | | | | | | |
| CCB | att | tac | aac | tgc | ggg | aga | ttg | ctg | gac | ata | taa | tgg | aat | ttt | CCC | aag | ACC | agc | atg |
| Ъ | H | × | z | ່ວ | ່ ບ | ~ | Ţ | Ţ | Ω | | * | 3 | z | 5 4 | 4 | × | H | ß | × |
| œ | ! | H | H | K | 9 | Q | ນ | 3 | E | × | z | 9 | H | Έđ | СI | ~ | а | K | 3 |
| z | 1 | Ø | 1 | × | 团 | ₩ | ¥ | ರ | H | H | Z | Ħ | 5±, | Ø | ø | Ω | Ö | H | Ü |
| 2641 | 1/88] | | | | | | | | | 2671 | /891 | | | | | | ! | | |
| ggt | CCA | gat | tca | tta | agc | tga | aac | tgg | agg | gtg | cca | Cac | cag | atg | agc | dcc | aga | ttg | tat |
| ဗ | а | <u> </u> | ಬ | 드 | ល | * | z | 3 | ្ត | · > | <u>a</u> | Ħ | Ö | ı | ໝ | | ໝ | ı | ß |
| > | Œ | H | = | ß | K | 터 | H | Ö | ø | ບ | Ħ | E | ಬ | * | Ø | а | Ø | ບ | , _ |
| ß | H | <u>5</u> -1 | H | œ | Γ | × | 1 | 된 | ~ | K | H | Д | Ø | 妇 | ĸ | œ | 1 | > | 노 |
| 2701 | [/80] | _ | | | | | | | | 2731 | /911 | | | | | | | | |
| tca | atg | aaa | tac | tca | agg | ctg | cct | acc | aac | toa | tgg | tgg | atg | tgt | ttg | gta | att | acg | tca |
| တ | E | × | ಬ | ಭ | × | Ţ | 24 | Ħ | z | Ω | X | 3 | X | ບ | ı | > | Н | H | Ω |
| œ | * | z | ď | ы | 9 | ນ | П | а | E | Ħ | Ö | ೮ | ບ | > | 3 | * | Ţ | ~ | = |
| z | 되 | H | L | ø | ¥ | K | > | œ | ᆸ | Z | > | Ω | > | <u> </u> | Ö | z | × | > | H |
| 2761 | 1/92 | | | | | | | | | 2791 | 1/931 | | | | | | | | |
| tta | aga | agt | tct | ttg | aat | ttg | gca | gtc | ttg | aac | aga | agc | tgg | ctt | tgg | cag | aac | gga | tta |
| Œ | ~ | ಬ | ಬ | 17 | z | ŗ | æ | > | 'n | z | ~ | ß | X | 1 | ≥ | a. | z | _o | 泸 |
| හ | E | > | Г | * | Н | × | ď | ಭ | * | EH | E | 4 | Ö | ĬZ4 | ೮ | × | E | Ω | ಬ |
| ď | × | بتز | Ŀ | H | Ē | Ü | ß | 17 | 田 | ø | × | Н | Ø | 1 | K | H | ~ | H | ~ |
| 282] | 1/94 | _ | | | | | | | | 2851 | 1/951 | 4 | | | | | | | |
| gag | dcc | acg | tcc | tgt | cat | tgg | cac | tac | aga | tgt | atg | gat | dcc | gtg | tta | tec | aga | aag | ctc |
| ঘ | Ø | E- 4 | ಬ | - | | 3 | = | × | × | ນ | X | ¥ | æ | | _ | ಬ | يم | × | Ţ |
| ĸ | Д | ~ | d | > | H | g | Ħ | H | Ω | > | 3 | Н | Ъ | - 1 | × | Y | 뇬 | ß | ន |
| G H V L | H | > | 1 | ß | 7 | K | ᆸ | œ | A L Q M Y G C R | × | ೮ | ບ | ĸ | > | H | œ | × | ¥ | ļ |
| | | | | | | • | | | | FIG | 18 | Ŀ | | | | | | | |

| 28 | 91/18 | - | | | | | | | | 2911 | /971 | _ | | | | | | | 2881/961 |
|----------|------------|-----|-----------------|----------|----------|-----|-----|------------|--------|-------------|----------|-----------------|-------------|----------|----------|--------|----------|-------------|----------|
| r t | g agt | tta | tta | ctt | cag | acc | agc | aga | atq | AGA | tag | tta | dad | aac | tad | ato | מככ | ato | +0+ |
| 7 | S | Ţ | ſΣ., | 1. | ď | E | ູໝ | ' ≃ | , ≅ | , ∝ | ** | بتزا | ່ງ | z | * | ` = | | n . × | i i |
| * | > | X | Ŋ | 54 | × | գ | ¥ | 妇 | * | ۵ | | ູເລ | g | : = | ~ | : 3 | ۵. | : 2 | <u>,</u> |
| _ | # . | H | ď | ß | Ω | C | 0 | Z | £ | Σ | > | ~ | , fe | ٠, - | : - | : " | , = | , > | ; - |
| 29, | 11/98 | 7 | | | | ł | ł | ; | l | 2971 | /991 | • | 1 | 1 | į | , | • | • | 1 |
| tgı | a agt | gtg | tga | aag | ato | aga | atg | gca | ato | acq | tad | tta | aga | aat | qca | tta | aat | ata | tac |
| * | တ္ | > | * | × | — | × | Σ | ¥ | H | | · · | ĵ z ., | , ≃ | z | · « | , I | z | , , , | × |
| 曰 | > | ບ | Ħ | ~ | ಬ | Ħ | 3 | Ø | ಬ | ~ | 9 | ໝ | [2] | Σ | = | * | Σ | ບ | £ |
| - | ر د | > | × | a | ø | z | ŋ | Z | = | > | > | Ö | × | ບ | — | Œ | ני | > | , c |
| 30(| 11/10 | 01 | | | ! | | | | | 3031 | /101 | · | ; | ŀ | ŀ | l |) | • | ĸ |
| agc | cac | agt | ctt | tgc | aat | tta | tca | tag | atg | cgt | tta | agg | gac | agg | tat | ttq | act | tat | CCB |
| တ | д | S | I. | ບ | z | T | ß | အ | × | . × | 1 | * | , <u>a</u> | E | X | Ľ | ď | × | Д |
| 4 | d | > | Ē | 4 | H | × | = | × | ບ | > | * | g | Ħ | 9 | H | ပ | 1 | H | = |
| # | ď | ß | , , | œ | <u> </u> | H | H | Ω | K | <u>5-</u> 4 | × | හ | Ø | > | Ē | 4 | H | ಬ | E |
| 306 | 51/10; | 21 | | | | | | | | 3091 | /103 | _ | ľ | | | | | | |
| CAC | atc | ctt | atg | gct | gca | gag | tga | tta | aga | gaa | tcc | tag | ago | act | qtc | tcc | cta | ACC | AGA |
| = | H | ц | X | Ø | 4 | ম | * | F | 2 | E | S | × | ំន | T | · > | ಭ | , 1 | E+ | ໍ່ແ |
| = | ಣ | H | 3 | 'n | പ | ß | Ω | ಬ | 띰 | z | <u>Q</u> | Ö | æ | 17 | ಬ | а | * | Д | ۵ |
| | <u>a</u> | ⊁ | ರ | ບ | ĸ | > | H | ø | ~ | H | 1 | 妇 | Ħ | ບ | 1 | d | 0 | C | E |
| 312 | 1/104 | 41 | | | | | | : | | 3151, | /105 | -4 | | | | ı | i | ł | ı |
| cac | tcc | cta | ttt | tag | agg | agc | ttc | acc | agc | aca | Cag | adc | agg | tta | tac | add | atc | aat | ata |
| = | ಭ | ľ | Ē£. | * | × | S | ĮŦ1 | = | ູໝ | | o o | ູ່ຜ | ່ຜ | , I | × | ; ≃ | H | z | , E |
| H | а | X | ž | × | ပ | ø | ß | 4 | ¥ | = | ĸ | æ | × | ပ | E | Ö | ß | H | × |
| ⊶ | d , | H | Ţ | 臼 | 团 | Ţ | = | œ | ≕ | H | 田 | Ø | 1 | > | O | Q | Ö | × | ಶ |
| 318 | 1/106 | 51 | | | | | | | | 3211 | /107 | | | | ł | | ł | | |
| gaa | att | atg | taa | taa | aac | atg | tac | tgg | aga | acg | gta | gtc | ctg | agg | ata | ава | dca | aaa | ttq |
| FI | Ι | Σ | * | S | z | X | × | 3 | ໝ | E | > | > | | 2 | · | × | 4 | × | |
| ¥ | 7 | ບ | Z | а | Н | ບ | Ξ | ප | Ø | ~ | ß | ಬ | * | ප | * | × | œ | z | ບ |
| Z | ⊼ | > | | œ | 7 | > | ı | 闰 | = | ರ | ~ | Q. | Ħ | Q | × | ß | × | H | > |
| 324 | 1/106 | 31 | | | | | | | | 3271, | /109 | , 4 | | | | | | | |
| tag | cag | aaa | \mathbf{t} cc | gag | gca | atg | tac | ttg | tat | tga (| gta | agc | aca | aat | ttg | caa | gca | atg | ttg |
| * | ŏ | ¥ | ಬ | 퍼 | ~ | Σ | X | | >1 | * | > | SQ. | E | z | Ţ | O. | A | × | L |
| ಬ | ~ | z | ď | × | Ö | ບ | Ŧ | ບ | H | 田 | ស | Ø | ď | H | ນ | × | Ö | ပ | ບ |
| ~ | E | H | ~ | Ü | Z | > | 1 | > | 1 | W | œ | Ħ | × | ĮΞĄ | ¥ | ಬ | Z | > | > |
| | | | | | • | | | | | | 40 | | | | | | | | |

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al. Inventors:

gtg ttg act tag ggc cca tct gtg gcc ccc cta atg gta tca tct gag gca gtg tca ccc gct gtt ccc tca ttc ccg ctg acc tca ctg I, M V S S E A V S P A V P S F P I, T S I, aat gtt cta gtg tag agt ctg aga cgg gca gta agt aca cct atg gca ago aca ttc tgg tgg aga agt gtg tta ctc acg cct cac gta cgg agc gcg ctg tgc tca tcg atg agg tgt add agt atg ata aga too ggo coo aca tog caa cto tto cca ago tgg aga agt act aca tga aga acg P S W R S T T * R T ged cae tgg caa atc caa eca gea acc aga 3541/1181 3481/1161 3601/1201

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al.

Inventors:

agt ggt tgo tco agg att act cco tco tco aga aga aga ato aga tco acg agt gga aga aaa aaa aga aaa aga aaa ggt ttt K K K K K G K G F aaa tga, ccc caa att tgc ctg gcc ggc aag ttt tgc aaa tag ctc ttc ccc acc tcc tta 3751/1251 3991/1331 god ttt gta aat tta att tta tta cad ata ada tgt aca aac aaa aac aga gaa T N K N K K T * E ggt tta aca aaa aaa aaa agc ttt aaa ged ada tat ttt gtt dad tgt tgt gee otg etg ttt tac tgg tgt 3901/1301 3841/1281 3961/1321 4021/1341

| | att taa cac tgt tta taa aaa ata tat ata tat ata tat ata tat aat gaa aaa ggt tto | ž, | ಭ | œ | | ttt | Ŀ | Ŀ | <u>a</u> | | gaa | 阳 | z | H | | BABC | z | T | = | | l gta | > | ಬ | r F | | gta: | > | * | S3 | | tac | × | 1 |
|-----------|---|---------------|-------------|----------------|-------|-----|-----|-----|-------------|------|-----|----------|---|-----|-------------|------|----------|-------------|----------|-------|-------|----------|---|--------|-------|------|-------------|-------------|-----|-------|-----|----------|---|
| | ggt | Ü | > | 124 | | cct | ď | ij | 1 24 | | CCB | بم | ø | 14 | | att | H | 1 | ~ | | ttc | ı | 3 | 0 | | tt | Ē | 1 | _ | | act | H | : |
| | 888 | × | × | × | | atg | Σ | ນ | K | | Cad | = | Ħ | ם | | tct | ಭ | ч | X | | ctt | ,J | Ē | æ | | aaa | × | z | H | | cga | ~ | 1 |
| | gaa | ⊭ ⊒ | × | × | | aaa | × | × | Z | | gag | 퍼 | ß | K | | ttt | Æ | بخا | 1 | | ctg | Ţ | ບ | 4 | | tac | × | = | œ | | agt | S | , |
| | aat | z | Σ | * | | taa | * | × | × | | tga | ပ | ø | 24 | | ttt | æ | ĬΞ | Ħ | | act | £+ | 1 | ß | | ata | ; | > | H | | agt | ಬ | |
| | tat | × | — | * | | ttc | ĮT. | ಬ | П | | aga | ~ | Ω | X | | gga | U | ۵ | H | | CCA | ч | Ö | z | | cat | = | H | × | | act | 4 | |
| | ata | ⊢ | × | } 4 | | ава | × | z | H | | agg | ĸ | G | स्र | | act | H | 1 | 3 | | aat | z | H | ß | | ttg | Ţ | ບ | K | | tac | × | |
| = | tat | > + | H | × | | atg | × | * | 冠 | - | agg | × | ಅ | 되 | - | cct | e4 | ı | × | 1 | aaa | × | × | ¥ | 1 | act | Ħ | ı | ĮΞι | - | atg | Z | |
| 4171/1391 | ata | | × | H | /141 | ttt | Ē. | ı | ≯ | /143 | gtg | > | * | 퍼 | /145 | ctg | | ນ | K | /147 | aaa | × | × | × | 1/149 | tag | * | × | Ω | 1/151 | ata | H | |
| 4171 | tat | > | ; | ≯ | 423] | aag | × | ಬ | > | 4291 | ttc | ĮŦ. | ß | ~ | 4351 | tta | T | × | H | 4411 | gag | H | × | 闰 | 447] | gtg | > | ບ | > | 453] | tat | ಣ | |
| | ata | H | × | Ħ | | att | ĭ | יו | * | | ctg | 1 | ນ | > | | tgt | ່ນ | > | <u> </u> | | cat | = | Σ | * | | ttg | T. | 3 | Ö | | gta | > | |
| | tat | > | H | × | | gac | Ω | Ħ | Ξ | | agg | ~ | Ö | Ø | | gat | Ω | | 1 | | tag | * | ß | 4 | | tac | > | Ħ | ı | | tct | ಬ | |
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| | tta | -7 | > | Ħ | | gct | 4 | П | <u> </u> | | tta | 1 | X | Σ | | ctg | ľ | 3 | Ü | | aat | Z | Η | ß | | ata | H | × | H | | ttt | jari | |
| | tgt | ಲ | > | Ħ | | ава | × | × | ಬ | | ata | ⊢ | × | H | | agg | × | ဗ | Ø | | taa | * | × | × | | taa | * | × | Z | | tgt | ່ນ | |
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| 4141/1381 | taa | * | z | T | 1/140 | gtt | > | 1 | Ö | /142 | gag | 田 | æ | a | /144 | ctt | 7 | 드 | <u>1</u> | ./146 | gaa | 阳 | × | × | 1/148 | ctt | 7 | <u>54</u> | ß | 1/150 | ttt | Ŧ, | |
| 4141 | att | _ | تحا | L | 4201 | aga | × | 田 | ß | 4261 | ttg | ; | 3 | 9 | 4321 | cgt | ~ | > | S | 4381 | att | H | 7 | * | 444] | ttg | 7 | ບ | < | 4501 | gta | > | |

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| 4561 | ttt tga ttg tac aat tgt aca ttt gta tac ctg taa tgt aaa tgt gga gaa gtt tga atc | ı. | Ē. | 7 | 4621 | aac | z | H | Ξ | 4681 | att | - | দ | Ω | 4741 | aga | × | Ħ | × | 4801 | AAA | × | × | × | 4861 | tct | ಬ | Г | * | 4921 | ttt | ш | 红 | 7 | |

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al. Inventors:

| 561 5011/1671 | aga | ء د | 2 | Σ | | act | a, | 1 | ы | | ttt | H | į | Ŋ | | tat | ີ ບ | > | × | | tgt | ່ນ | > | ೮ | | | | | |
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| 4981/1661 | aca atc T I | S) | | Z | 1/168 | act | - | -7 | ບ | 1/170 | ttg | 77 | * | 딾 | 1/172 | atg | Σ | * | 田 | /174 | ctt | r. | 13 | X | /116 | atc | V I F I L K N T | ಬ | ŗ |
| 498 | aca T | С | . 7 | Ζ. | 5041/1681 | tga | * | Ħ | z | 5101/1701 | tgt | ນ | > | 뇬 | 5161/1721 | CCB | d. | œ | Z | 5221/1741 | atg | N L M P G Q L F | ນ | ¥ | 5281 | gtg | > | * | Ω |

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, et al.

Inventors:

AAA GAG TAC AAA GAC AGC ACA AGA AAA AAA TTC AAA GAC ATT TCC AAC AAG GAA AGT. TGC
F K D I S N K E S C
S K T F P T R K V A
Q R H F Q Q G K L I 271/91
ATT CCA GCC GGC ABA TAA ATT CAA GAA GAA GAG AAA ATT CCA GCC AGA TGG TAG AAG CGA I P A R W * K' R F Q P D G R S D S S N Q I N S T R E N S S Q M V E A M
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 GGA AGT TAA AGG GAA AAA GCA ATT CAC AGG GG S A R F K A I H R B F F V K G F T G K S N S O F

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

TGA CTT CAA AAA GAA GAA AGA ACT GAA * I. Q K E F F P

FIG. 191

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente, et al.

| Table Tabl | | GA | | 더 | Z | , | AA | | × | Z | | CA | • | = | H | ; | GA | * | D | F | ŧ |
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| TCA GTA TGG TAA TGA ACA ACA SCA SCA SCA SCA SCA SCA SCA SC | | ACA | ⊱ | ¢ | α, | | AAA | × | Z | | | AAG | × | S | | | GTJ | > | > - | _ | • |
| TCA GTA TGG TAA TGA ACA ACA SCA SCA SCA SCA SCA SCA SCA SC | | AAA | × | × | Z | | GAG | 田 | × | ল | | CAG | ď | ~ | घ | | GGA | C | ध्य | Ü | 3 |
| TCA GTA TGG TAA TGA ACA ACA SCA SCA SCA SCA SCA SCA SCA SC | | BAG | r-7 | × | E | | TTC | بتز | S | æ | | AAT | z | } (| S | | CGT | ~ | > | C | = |
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| 541/181 TYCT GAP C D V I A S 601/201 T A L R C E 661/221 ATT TYCT I S 721/241 CGT GAG R V R V R V R | | CCA | d | С | x N | | AGA | ~ | . c | × == | | CAT | : :: | : = | : 0 | | CAA | E | : ≒ | < | ~ |
| 541/ TGT C V A 601/ ATT I L C 661/ ATT I C 721/ CGT | 181 | GAT | Ω | , | S | 201 | CCG | æ | ; ≃ | ं ध्य | 221 | մեն | ٠ د د: | نـر نـ | : ^{ເລ} | 24.1 | GAG |) | : - | _ | ပ |
| | 541/ | TCT | ت ت | > | * | 601/ | ATY | } | <u>-</u> | ຸບ | /199 | Arm | ; ; ;— | <u>.</u> | <u>.</u> | 721/ | CGT | : : | ; > | > | ⊀ |

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Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

GAC GGA AGA GCT CTA TGG GAA CAC ATT TYCA GAT TOT AAC TOO AAT GGO COA AAA GGA AGO CAA ACT CAG ATC AGA AAT GAT TGA AGC CAT CCG CGA AGC GGT GGT CTA CCT GGC ACA CAA AGC CAT TIT GGA GCA GAG GAA CAT GCT TGT GAT TAA GCA CTC ATT GGT GCA ATT AGA

Title: Genes Determining Cellular Senescence...

CAT AGT AAA TGA CAA ATA TGG AAG GAA GGT

CAT' ATC AGA AAT 'TAT' CAG T'T'C ATT' GCC TAG

1261/42

Leonard P. Guarente, et al. Inventors:

CCT GTG GCA TGG CAC GCC CAA GGA CAG GAA TICA AAA GGT GGC TAA TIGG CCA ATA CITC CCA TAC TAN GCT TGT GAA GCA GAT AAT ACA CGA TYG CGC CAG AGT GGC CAT GCA CTG ACT GAT TGT GAA AAC AAT GAA GAC TTA TGT TYP GGT TYP ACT GGC GGC ATT TGA TYG

CCT AIT GIA CIT ACT AAG CCC CAG AGA ICC IGC ACA IAC:AGT AGG AGA AAT CAT IGA AGT 1321/441

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

THE GUN AAA MEG AGA TEG AAA TEC ACA CAG TAA GAA MEA TAC AGA EGT CEG CAG ACG GGA GCT CCT AGA ATC CAT TTC TCC AGO TTT GTT AAG CTA CCT. GCA AGA ACA. CGC CCA AGA AGT TGA CAT TCT GGG ATC TGC CAC TGG AGA CGT TYA GCC TAC CAT GAA TGC CAT CGC CAG CTT GGC AGC AAC AGG ACT GCA TCC TGG GTT GGT GTC GGT GCT AGA TAA GTC TGC GTG TGT 1441/481 1501/501 1561/521

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

CCT GGA NGT TGC ANA CAN AGT CAN AGC TGC ACT GAA AAG CTY GAT TCC TAC ACT GGA AAA AAC CAA AAG CAC CAG CAA AGG AAT AGA 'AAT TICE GAG NGA AGG TITG TITT TIGG AAA AAC ACT THE THE MEG MEA THE AGT THE GAA GING GIT TOT AGA GOA TOT TOG TAT GAA GAA COT GAA GTO CITG GGO TAG TOT AAA TOG AGG TOO CAA GGA CGG MGA GCT TYCA CAT TYC AGA ACA ANT AGA GCA NGA TAA AAA GAT GAA AGA AAA TAT TOT THE TAG COT COT COA GAG THE TEA 1001/601

FIG. 19G

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

TCT ACT TGA AAA ACT GAG CAC ATA GGT GGA AAG AGT TAA GAG CAA GAT GGA ATG ATT TYT TOT CITY CITY TOT TOT GIT TOO CAA TGO AGA AAA GAA GGG GTA GGG TOO ACO ATA OTG GTA AIT! GGG GIRA CITC TGI! AIRA ITGI! GITF 'ITCI! ITCI! ITGI IRI! ACG AAF CITA ITIT. AIRA IRAA AITI GITI 2041/681 2101/701

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarente, et al.

| 95 | 4 172 8 | 262 9 | 346 5 | 4 35 | 524 15 | 624 | 704 | 779 | 845 70 | 929 95 | 100 4 120 | 1079 1456 | 1154 | 1229 195 | 1304 220 |
|--|--|--|---|--|---|--|--|----------------|-----------|----------------|---|--|--|---|--|
| 1 GGATCCCTCTGTGAGGCCGATT ATG CAG GCC TAG ACCCGCACGTGACCA CTTCGAGAGCAAGTTGCCTGCGAGTTTCTCTGCCGAGGAAAAAAA 1 | 96 A ATG GAG GCA ATT TAC TTA ATA TGG TAT GAG AGG ATC TTT TGA CGGCAAATAG ATG CGC CAT CTC CGA GAA AAA ATC 1 M E A 1 Y L I W Y E R 1 F * | TAG ACAATAACAGCGACAATTAACCTAAAGAGGATAGAAGATCGAGCAAAAAAATTTTTAAT ATG GGG TCA GTG GCG AFA TTA TAC TAT * | GTGGTAGAATT ATG ATT GAA CTC CGA AAC TAA GCGCCGATT ATG GGT GGC AAA GCG | GAC AGC TTT TGA TATATAATCGATCGCTCTCGTAGTTGATATCCTCTCTTTATCTTTTCCTGTATATAGTAT ATG TGT ACA TAC D S F * | 436 AGA TAC GAA TAT ACC TCA GIT AGT 'FTG TT'F TAA CATTAAATATTCAACAGCAGTAGCAAAAAAGAATATATCCATTCATT | 525 TTTTTCGTCTCATTACTGATATCCAACTAACAGTCTCCTCATAGACGGTACCTTACTTTCCTTTAATATTAAAATACTAGTATAGTCGCACATACTTAAC | TCGTCTCTCTAACACATA ATG AAA ATT TCC GCA GCT TTA ATA TTG TCT TCC CTT TCT GTC GCA TTT TCT GCC CCT | CT GTC ACT CAA | AAG K | GTA AAC V N | 930 GGT ATA GTT TCC TTG GAC TGG CTA GGA TTT GGT GGA TGG GCC TCT GTC ATG GAC ATG GAT GCC AAC ACT TCG TCC 96 G 1 V S L D W L G F G G W A S V M D M D A N T S S | GAA TGT AAG GAT GGC TAC TGT TCT TAT GCA TGT GAA CCT GGA.ATG TCA AAG ACT CAA TGG CCT TCT GAC CAA E C K D G Y Y C S Y A C E P G M S K T Q W P S D O | CCA AGC GAT GGT AAT GGT GGT CTT TAT TGT AAA AAT GGT TAC TTG TAC CGT ACC AAC ACT GAT ACC AGC PSDGKSV CT RSV GG LY CK N GY LY RT N T D T S | GAT TTA TGT TCT ACG GAT GAA ACA TCT GCT AAG GCC ATT AAC AAA AAG TCT GAC TCC ATT GCT CTA TGT AGG ACG D I. C S T D E T S A K A I N K K S D S I I A L C R T | GAT TAC CCA GGA TCT GAA AAC ATG GTG ATT CCC ACA GTG GTT GAT GGT GGA GAT TCA CAA CCA ATT TCA GTC GTT D Y P G S E N M V I P T V V D G G D S Q P I S V V |
| | | | - | . • | • | _, | _ | | | J. | on. | 1005 | 1080 146 | 1155 | 1230 196 |

Title: Genes Determining Cellular Senescence... Inventors:

Leonard P. Guarente, et al.

| 1379 245 | 1454 270 | 1529 295 | 1604 320 | 1685 1 | 1760 26 | 1838 5 | 1913 30 | 1998 5 | 2072 23 | 2160 3 | 2245 15 | 2331 10 | 2406 35 | 2457 10 |
|---|---|---|---|--|--|--|---|--|--|--|--|--|---|--|
| 1305 GAT GAA GAC ACT TAT TAT CAA TGG CAG GGT AAA AAG ACT TCT GCT CAG TAC TAT ATT AAC AAC GCC GGT GTA TCT 1221 D E D T Y Y Q W Q G K K T S A Q Y Y I N N A G V S 2 | 1380 GCA GAA GAT GGG TGC ATT TGG GGT ACT TCT GGT TCG GAT GTC GGC AAC TGG GCT CCA CTA GTG TTA GGT GCT GGT 1246 A E D G C I W G T S G S D V G N W A P L V L G A G Z | 455 TCC ACT AAT GGA GAA ACA TAC TTG TCG TTG ATT CCA AAC CCC AAC AGT AAC CAA GCT GCC AAC TTT AAC GTT AAA 1 271 S T N G E T Y L S L, I P N P N S N Q A A N F N V K 2 | 530° ATA GTT GCA TCC GAT GGC GCT AAC GTT CAG GGC AGC TGT GCG TAT GAA GAT GGC TCT TTC ACC GGA GAT GGT TCC 1 296 I V A S D G A N V Q G S C A Y B D G S F T G D G S | 605 GAT GGT TGC ACA GTT TCT GTT TTA TCT GGA TCT GCT GAA TTT GTT TTC TAT TAA GTCACTCTTCTTTCGGTAAAAGA ATG 321 D G C T V S V L S G S A E F V F Y * | TCT TGF ATT TTG ATA CCC TCA ATT CCC CTT ATT ATT CTT CTG CTC TCT ATT TAT TAT TAT ACA TTG GGAS ${ m S}$ C ${ m I}$ ${ m L}$ ${ m I}$ ${ m I}$ ${ m P}$ ${ m L}$ ${ m I}$ ${ m II}$ ${ m III}$ ${ m III}$ ${ m III}$ ${ m III}$ ${ m IIII}$ ${ m IIIII}$ ${ m IIII}$ ${ m IIIII}$ ${ m IIIII}$ ${ m IIIII}$ ${ m IIIII}$ ${ m IIIIIII}$ ${ m IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII$ | TTC CGT TAT ATT TTT CTC CTT TCA GTT CAT TTT ACT TCT TAA AAAGTTTCG1TGATCGCTATT ATG CTA TGG ATT CAA F R Y 1 F L L S V H F T S * | 9 AGA TIT TC'T 1'T' CTC TCT CTT CAA GGT G'TA CTC TGC ATT ACG GTT TTC TTT AGT TCG TTT ATT TTT TTG TTA 5 R F S F L S L Q G V L C I T V F F S S F I F F L L | ACA AGG TGT TTG TAT ACA TAT ATA ATAT ATG GAA ATA TTA TAG TGTTTATTTTGTTACTTCCTGCGAGTTGCAACAAACTA T R C L Y T Y I * M E I L * | 9 ACAAG ATG CCA TGC TGT TTT TCA TTT TTT GGC TAT AAA AAT AAC AGT ATC CTA GTC CTT GTG TTC GGC TTT 1 M P C C F F S F G Y K N N S 1 L V L V F G T | AAA ATG GAA TTG CAA ACC CCA TAA TTCCTTCTTCACACCGACAAACCGCCTAGTAGTCGATTTTCAGAGACTCTA ATG CTT TGA ATA K M E L Q T P * | 61 TAATTTTTTTTTCTTCAAAAATTTCCTTAAGCGTGCTATCGA ATG AGT AGA CAT CAA TCA AGA GTT TCA TGG TCT CCC CGT ATT TGC 1 S R V S W S P R I C | CGC TGC TTC TAA TATTTTGGAGTGTAGCATAGCCCAATCAATCAAATCTTCGATA ATG CCA CTT TTT ACA TAT ACA CGA CGA CAA R C F * | CCC ACA GTA GTA ACA CTC ATG ACT AAA TTT TCA TCA GTA CTT AAT GTC ATG TAA GGG GCT AAC GAA ATC AAT GCA ' | A'IG GGC GIT TCT CTA TAA ACG ATG ATA TGG GTA TTG TTC ACC ACT GGA TCC |
| 13 2 | 13 | 14 | 15 2 | 16 3. | 1686 2 | 1761 27 | 183 | 1914 31 | 199 | 2073 24 | 21(| 2246 16 | 2332 11 | 2407 36 |

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente, et al. Inventors:

| | | , 19 , 256 | 331 | 69 | 3 501 | 2 2 2 2 3 3 4 4 4 4 4 4 4 4 4 4 4 4 4 4 | 6 | 664 34 | 739 | 53 814 | 84 | 109 | 964 134 | 1039 | 1114 | 1189 | 1264 234 |
|--|--|---|-------------|--|--|---|---|---|---------|--|---|---|---|---|---|---------------------------------------|--|
| 1 TGTTTTAGTGCTACCCAACTACTTACATTCCTTTAAAAACCAATATTTAAAGTTTAAAGTTTAAACTTAAAATATTTTAAAATATTTTAAAAAAAA | 101 TACACCTTTACAATCCGTATTGCC ATG AAT ACC AAG GCT TGC TCA GCT TCT GCA GCA GTT CAA CCC TTT CCA ATA CCG CCA | TAT TIT TGG TIT TAT CIT CGT TIC TIT CTC CTG A | L L GCC TTT | F S K S G H A F F ACC AGA AAA TAG CCATTA ATG CTT T | L K K * M L TGGTTTGCATTTGGAAAGGTTTTGTGTAAGAAAAGCAATACTT | 502 AAAACAAGAGAAAAAAAACACTTTACTAATATCCAATCCTTTATTTTTTGCAGAA ATG AAA TTC TCA ACT GCC GTT ACT ACG | TTG ATT AGT TCT GGT GCC ATC GTG TCT GCT TTA CCA CAC GTG GAT GTT CAC ACC ACC GTG GAT GTT CAC ACC ACC ACC ACC ACC ACC ACC ACC A | AGG GCC GTTP GCC TRACE STATE TO B A LE P. H. V. D. V. | R A V A | SEVA TO TO THE GOT ACT TO THE ATT ACA ACA TOT GIG TIG GOT COA ACC TO GOA GOO GOT | GGG ATA GCC GCT TCC ATT GCT GTT TCA TCT GCT TGC TTA GCC AAG AAT GAG AAA ATC TCT GAT GCC GCT GCA TCT | GCC ACT GCC TCA ACA TCT CAA GGG GCA TCC TCC TCC TCC TCC TCC TCC TCG GCA ACT TCT ACA TCT TCT ACT ACT ACT ACT A | TCT GTT TCT TCA TCT AGA GAN GAN GAN GAN GAN GAN AGC AGC | S V S S S E E A A P T S T V V S T S A T P C S S S A T Q S S S S S S S S S S S S S S S S S S | A S S A T K S S T S S T S P C T T S T S P C T S T S T S T S T S T S T S T S T S T | S S S S S S S S S S S S S S S S S S S | GAC TYT TCA GGC CCA AGT GAG AAA TTC GAA GAC GGC ACT ATT CCA TGT GAC AAA TTC CCA TCT GGT CAA GGT GTC D F S G P S E K F Q D G T I P C D K F P S G Q G V |
| | 1 | П | 2 | e . | 4 | | 590 10 | 99 | 35 | 60 | 815 85 | 890 110 | 965 | 13 | 160 | 1115 | 210 |

| 1265 ATT TITT AND THE | | 1339 | 1414 | 284 1489 | 309 1564 | 334 1639 360 | 1714 | 686 | 4.9 | 13.9 9.9 | <i>y</i> | 90 | 2150 |
|--|------|------------|-------------|------------------|--------------------------|--------------------|-------------|-------------|----------------------|--------------------|-------------|-----------------------------|------------|
| AND GROUND AND THEY THEY THEY THEY THEY THEY THEY THEY | | | וה ע | 5 7 | Ä H | 7 7 | , H | | # FI | 4 H | 4 C/4 | 21 | 21 |
| Name | | TGC | rct | TTA | L TAC V | CAA | GAA | ACT | GTT | 366 | rtt | | |
| Name | | TCA | CCA | TAC | | | | | | | rttr | | |
| Name | | GGT | CAA | GAT | | | | | | | CCTT | TGT | |
| Name | | 299 | | | | | | | | | , , | $\mathtt{TAC}_{\mathtt{Y}}$ | |
| Name | | ACT | TCC | | | | | | | | CTAC | TTA L | |
| Name | | TCC S | CCA | ACT | | | | | | | ACTAC | TAT Y | |
| Name | | ACT T | TGG W | AAC N | | | AAC | AAC . | AAC | rTC 7 | cara | CGA R | |
| Name | | GAC D | CAA | TCT | | | | TTA | TTG . | | 3CTA | TAC Y | |
| AAG GAG GAG TCC TAC TGC TAC TCC TAC TCC TAC CAA CCA GGT ATG TCC AAG GAA AAC GAC GAG TAC TCC TAC TCC TCC TCC TCC TAC TCC TAC TCC TC | | | | CGT | :: GGT G | | | | | | | | |
| ABG GAG GGG TCC TAC TGG TTG TCC TAC TCC TGC CAA CCA GGT ATG TCC TAC TCC TAC TCC TGC CAA CCA GGT ATG TCT TCC TAC TCC TGC CAA CCA GGT ATG TCT TCC TAC TCC TGC CAA CCA GGT ATG TCT TCT TGC TAC TCC TGC CAA CCA GGT TAT TTG TCT TGC TAC TCC TC | | | • • • | | - AAG K | AGC S | TAC Y | GCA A | | | | | |
| AAG GAG GGG TCC TAC TGT TCC TAC TCC TGC CAA CCA GGT ATG K E G S Y C C S Y S C Q P G M AAG GAG GGG TCC TAC TGT TCC TAC TCC TGC CAA CCA GGT ATG GAC GGT AGA TCT GT GGG GGT TTG TTG TGT AAA AAT GGT TAT C E M G V E A A Y V V S K L CCG GGC ACT GAA AAC ATG GTT ATC CCA A C TAT GTT GTT TCT AAA GGG GAT ACT TAC TTT ACT TGG GAA GGC AAC TAT GTT GTT GTT TCT AAA GGG GAT ACT TAC TTT ACT TGG GAA GGC AAC TAT GTT GGT AAC GAT GGA TCT GAA TCG GGG GGT TCT GGT TTG TCT GGT AAC GAT ACT TAC TTT ACT TGG GAA GGC AAC TAT GTT GGT AAC GGT GGA GGG TGT TCA TCG GAA GGC AAC TAT GGT AAC GGT GGA GTG TCT TAC TTG GGA TCT TCT GGT ATT GGT AAC GGT GGA GTG TCT TAC TTG GGT ACT TCT GGT ATT GGT AAC GGT GGA GTG TCT TAC TTG GGT ACT TCT GGT ATT GGT AAC GGT GGA GTG TCT TAC TTG GGT ACT TCT GGT ATT GGT AAC GGT GAT GAA TCC GGT ACT TCT GGT ATT GGT AAC GGT GAT GAT TCC AAT GC GGT AAC TCT GGT ATT GGT AAC GGT GAT GAT TCC TTG TCT GGT ATT GGT ATT GGT ACC G G G G G TCT TCT GTT ACT TCC GGT AAC TCT GGT TTC A A A D D D S S N V I S L S L I P N N N GCT TTTTTTCGAACACACTCACACACACACACACACACACACA | | | | | | | | TGG W | AGC S | GAA E | TAC | | |
| AAG GAG GAG TCC TAC TGT TCC TAC TCC TGC CAA CCAA AAG GAG GAG TCC TAC TGT TCC TAC TCC TGC CAA CCAA K E G S Y C S Y S C Q P GAC GGT AGA TCT GTC GGG GGT TTG TCT AAA AAT TGT GAA TGG GGT GTC GAG GGT TTG TCT TGT AAA AAT C E W G V E A A Y V V V GAT ACT TAC TTT ACT TGG GAA GGC AAA AAG ACA TCT GAT ACT TAC TTT ACT TGG GAA GGC AAA AAG ACA TCT GAT ACT TAC TTT ACT TGG GAA GGC AAA AAG ACA TCT G G C T T T T TCT GGT ACA TCC AAT GT ACA TCT G G C T T T T TCT TCT GGT ACT TCT GGT ATT GGT GGT GAT ACT TTA ACT TGG GAA GGC AAA AAG TCT G G C T T T T T TCT TTC TGG GAA GGC AAA AGG TAT GGT GGT GAT ACT TAC TTA TCT TCT GGT ATT G G C T T T T TCT TCT TCT GGT ATT G G C T T T T T T T T T T T T T T T T T | | | | | | | | | AAC N | TAC Y | TTA L | | |
| AAG GAG GGG TCC TAC TGT TCC TAC TCC TGC CAA AAG GAG GGG TCC TAC TGT TCC TAC TCC TGC CAA B | | | | | | GAA E | GCT A | GGT G | AAC N | GTT V | GTC V | | |
| APG GAG GGG TCC TAC TGT TCC TAC TCC TGC K E G S Y C S Y S C GAC GGT AGA TCT GTC GAG GGT TTG TTG TGT TGT GAA TGG GGT GTC GAG GGT TTG TTG TGT C E W G V E A Y V CCG GGC ACT GAA AAC ATG GTT ATC CCA ACC D G T E W M W V I P T GAT ACT TAC TTT ACT TGG GAA GGC AAA AAG G C T W G G T T G GGG GGT TCT GGA TCT GGT GGA GTG ACT TTA ACT TGG GAA GGC AAA AAG GAT ACT TAC TTT ACT TGG GAA GGC AAA AAG G C T W G T T G G GT ACT TCT GGA TCT GGT GGA GTG ACA TCG GGT ACT TCT GGA TCT G G C T W G T T T G T T G G T T G G T T T T T | | | | | | GT'T V | TCT S | ATT I | CCA P | $^{ m TGT}_{ m C}$ | TTC F | | CAT |
| AAG GAG GGG TCC TAC TGT TCC TAC AAG GAG GGG TCC TAC TGT TCC TAC BAG GAG GGG TCC TAC TGT TCC TAC CAC GGT AGA TCT GTC GGG GGT TTG CCG GGC ACT GAA AAC ATG GTT ATC CCG GGC ACT GAA AAC ATG GGT ATC CCG GGC ACT GAA AAC ATG GTT ATC CCG GGC TTT AC TTT ACT TGG GAA GGC D T Y F T T TCT TTTC GAT GTC GGT GGT GGA GTG TCT TAC TTG GGT TCT GGT GGA GTG ACT GGA GGT TCT GGT GGA GTG TTT ACT TGG GAA GGC GGT GGA GTG TTT ACT TGG GAA GGC GGT GGA GTG TTT ACT TGG GGT TCT GGT GGA GTG TTT TCT TTG GGT GCT GCT GAT GAT TCC ATT GTC A A D D S S N V TGT ACC GTC TCT GTT ACT TCC GGT CTTTTTTTCGAACACACTCTCACCCCTATACCT TTTT TCT TTT CGT TAA TGGCCTCA ATG F S F R | | | | | | | | GGT G | AAC N | gaa E | CAT H | CACT | TAC |
| AAG GAG GGG TCC TAC TGT TCC TAC AAG GAG GGG TCC TAC TGT TCC TAC BAG GAG GGG TCC TAC TGT TCC TAC CAC GGT AGA TCT GTC GGG GGT TTG CCG GGC ACT GAA AAC ATG GTT ATC CCG GGC ACT GAA AAC ATG GGT ATC CCG GGC ACT GAA AAC ATG GTT ATC CCG GGC TTT AC TTT ACT TGG GAA GGC D T Y F T T TCT TTTC GAT GTC GGT GGT GGA GTG TCT TAC TTG GGT TCT GGT GGA GTG ACT GGA GGT TCT GGT GGA GTG TTT ACT TGG GAA GGC GGT GGA GTG TTT ACT TGG GAA GGC GGT GGA GTG TTT ACT TGG GGT TCT GGT GGA GTG TTT TCT TTG GGT GCT GCT GAT GAT TCC ATT GTC A A D D S S N V TGT ACC GTC TCT GTT ACT TCC GGT CTTTTTTTCGAACACACTCTCACCCCTATACCT TTTT TCT TTT CGT TAA TGGCCTCA ATG F S F R | | | | | | | | | | GGT' G | | CAAT | ' CTG |
| AAG GAG GGG TCC TAC AAG GAG GGG TCC TAC K E G S Y GAC GGT AGA TCT GTC C E W G V CCG GGC ACT GAA AAC CCG GGC ACT GAA AAC CG GGC ACT GAA AAC GAT ACT TAC TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT C T Y GCT GGC GTG TCT GCT GTG TGT C T TTT TCT TTT TCT TTT CGT TAA TTTT TCT TTTT CGT TAA TTTT TCT TTTT T CGT TAA TTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TA | | | | | | | | | | | | r . | |
| AAG GAG GGG TCC TAC AAG GAG GGG TCC TAC K E G S Y GAC GGT AGA TCT GTC C E W G V CCG GGC ACT GAA AAC CCG GGC ACT GAA AAC CG GGC ACT GAA AAC GAT ACT TAC TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT C T Y GCT GGC GTG TCT GCT GTG TGT C T TTT TCT TTT TCT TTT CGT TAA TTTT TCT TTTT CGT TAA TTTT TCT TTTT T CGT TAA TTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TA | | : GAG E | TAC | TTG L | GCC | ATC | 9 0 | TCT S | $_{\rm L}^{\rm TTG}$ | GTC V | GGT G | racci | A ATC |
| AAG GAG GGG TCC TAC AAG GAG GGG TCC TAC K E G S Y GAC GGT AGA TCT GTC C E W G V CCG GGC ACT GAA AAC CCG GGC ACT GAA AAC CG GGC ACT GAA AAC GAT ACT TAC TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT GAT GGG TGT TTT ACT C T Y GCT GGC GTG TCT GCT GTG TGT C T TTT TCT TTT TCT TTT CGT TAA TTTT TCT TTTT CGT TAA TTTT TCT TTTT T CGT TAA TTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TAA TTTTT TCT TTTT CGT TA | | , ggc G | TCC S | GGT | GCT A | GTT V | GAA E | ACT T | TCA S | AAT N | TCC | CTA | CTC |
| AAG | | i ATI | rgi C | 9 9 9 9 | GAG | AT'G M | Ď E ₃ | GĞ | TTA L | TCC S | ACT T | ACCC | TGG |
| AAG | | Ö Z | TA. Y | ' GTC V | , GTC | AAC N | ACT T | TGG W | TAC Y | TCA S | GTT V | rctc | TAA * |
| AAG | | | 3 TCC | A TCT | GGT G | GAA E | TTT F | ATC I | ACA T | GAT D | TCT S | CACA | CGT R |
| AAG | | | | r AGA R | v TGG | ACT T | , TAC Y | TGT C | GTG V | GAT D | GTC V | CGAA | TTT F |
| | 100 | | G GA(| | r GAA | 9 666 | | 9 9 9 | GGA G | GCT A | ACC | TTTT | TCT S |
| 1265 235 235 1340 260 1415 285 1490 310 1715 385 17790 410 1715 385 1740 410 11865 435 12109 | É | I I | AA. K | GA(| TG | CCC P | GA1 D | GA1 D | GGT G | GCT A | TGT | CTT | TrTT F |
| | 1361 | 235 | 1340 260 | 1415 285 | 1490 310 | 1565 335 | 1640 360 | 1715 385 | 1790 410 | 1865 435 | 1940 460 | 2023 1 | 2109 15 |

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| Docker 1 to | 0050.1 171 005 |

| Doomer 10 | 0050.1 121 005 |
|--------------|------------------------------------|
| Title: Genes | s Determining Cellular Senescence. |
| Inventors: | Leonard P. Guarente, et al. |
| | |

| KKKKKKVRPH NFQCIHSLNF | 100 SRNSSMKLSA ALILSSLSSV SRNSSMKLSA LLALS | 150 AVVIPAA HTVTPAASEV | 200 AAATTSAAAS KISDAAASAT | 250 |
|--|--|---|--|--|
| KKKKKKPRPH | | EKPAVV TVTQYID DKRAVV TVTQYVNADG .KRAVAYKYV YETVVVDSDG -K-AVVT | TSVLAPTSSA AADGKVESVA ATTTTLSSTA | 250 EAAPTSTVVS TSSATQSSAS |
| PRSKLSKDFK PQFTLLSSVT | VYFLFTHSFL FEYNQLLVLP LNKNLPSLNF | EKPAVV TVTQYID DKRAVV TVTQYVNAD. .KRAVAYKYV YETVVVDSD | AATSTVES.A ATTTTI AADGKVESVA AATTTLSSTA AAADSSASTA VSSAALAKNE AAS-A | QDG'rVKC EDG'rISC ESSSVSSSSE |
| PRSKLSKDFK | FEYNQLILVI.P | DSHHEDHIKD VIHSDNIHIIN VHQEDANQH. | SN 'ITATSA TSVIJAPTSSA | TSEQKRDGGF SSSSVGSGDF SSSSSATSTL -S |
| MCFLETSAS | 51 VYFLF1H3FL | 101 AFSAPAPAPA ASTAVLAAPA ALVSALPHVD A | 151 SN 'rTALSA ATAATSATIT TSVLAPTSSA | 201 SSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS |
| Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus |

FIG. 22A

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

| 300 | GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC- | 400 IPTVVDGGDS QPISVVDEDT VPTVVGAGSS QPINVIKEDS IPTYVEGGSS I,PLTVVDODT -PT-VG-S -PVD- | 450 LVI.GAGSTNG VVL.GAGYTDG LNFGAASTGG |
|--|--|---|---|
| PGGWASVMDM I.GGWASIMDM SSSSSSSSSIVT | LYCKNGYLYR LYCKNGKLYR LLCKNGYLYR L-CKNG-LYR | TDYPGSENMV IPTVVDGGDS QPISVVDEDT TDYPGSENMV VPTVVGAGSS QPINVIKEDS TDYPGTENMV IPTYVEGGSS LPLTVVDODT TDYPG-ENMV -PT-VG-S -PVD- | 450 SGSDVGNWAP LVI,GAGSTNG EGSGVGNWAP VVLGAGYTDG SGSGIGNWAP LNFGAASTGG -GSGNWAPGAT-G |
| 251SDFPSV NGIVSLDWLG FGGWASVMDM STT.STSTSTSTSTSTSTSTSTSTSTSSSSSSSSSSSS | GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC- | 400 TDETSAKAIN KKSDSIALCR TDYPGSENMV IPTVVDGGDS QPISVVDEDT EGOGSAOAVN KVSGSIAICG TDYPGSENMV VPTVVGAGSS QPINVIKEDS WGVEAAYVVS KLSKGVAICR TDYPGTENMV IPTYVEGGSS LPLTVVDODTA K-SA-C- TDYPG-ENMV -PT-VG-S -PVD- | YYQWQGKKTS AQYYINNAGV SAEDGCIWGT SGSDVGNWAP LVI,GAGSTNG YYQWQGKKTS AQYYVNNAGV SVEDGCIWGT EGSGVGNWAP VVLGAGYTDG YFTWEGKKTS AQYYVNNPGV SVEDGCIWGT SGSGIGNWAP LNFGAASTGG YW-GKKTS AQYY-NN-GV S-EDGCIWGT -GSGNWAPGAT-G |
| SPSTSTSTST | GMSKTQWPSD GYAKTQWPSE GMSKTQWPSD GKTQWPS- | 351 TDETSAKAIN KKSDSIALCR EGOGSAOAVN KVSGSIAICG WGVEAAYVVS KLSKGVAICRA K-SA-C | AQYY INNAGV AQYYVNNAGV AQYYVNNPGV AQYY - NN - GV |
| 251 SATKSSTSST | GYYCSYACED GYYCSYACSD GSYCSYSCQD G-YCSY-C-P | 351 TDETSAKAIN EGOGSAOAVN WGVEAAYVVS | YYQWQGKKTS YYQWQGKKTS YE'EWEGKKTS YW-GKKTS |
| Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | File.1 (NCa3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus | Pile.l (Nca3) Pile.l (Uth1) Pile.l (Sag1) Consensus |

FIG. 22E

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al.*

| ETYLSLIPNP NSNQAANFNV KIVASDG.AN VQGSCAYEDG SFTGDGSDGC [TYLS11PNP NNKEAPNFNI KIVATDG.ST VNGACSYEDG SFTGDGSDGC VTYLSLIPNP NNSDALNYNV KIVAADDSSN VIGECVYENG BFSG.GADGC -1"YLS-TPNP NA-N-N- KIVA-D V-G-C-YE-GG-G-DGCSLIPNP NNGNALNFNV KIVAADDSST VNGECTYENG SFGGGG | Obdespecto |
|---|--|
| VQGSCAYEDG & VNGACSYENG VIGECVYENG E V-G-C-YE-G | |
| ETYLSLIPNP NSNQAANFNV KIVASDG.AN VITYLSLIPNP NNKEAPNFNI KTVATDG.ST VTYLSLIPNP NNSDALNYNV KIVAADDSSN V-TYLS-IPNP NA-N-N- KIVA-D V | |
| NSNQAANFNV NNKEAPNFNI NNSDALNYNV NA-N-N- NNGNALNFNV | 515 PVFYZ FVFYZ PVLYN PV - Y - FVLY. |
| ETYLSLTPNP [TYLSLTPNP VTYLSLTPNP -TYLS-TPNP | 501 'YUSVILSGSAE FUFYZ TVSVTSGSAN FUFYZ TVSVTSGKAH FULYN TVSV-SG-A- FV-Y- 'TVSVTAGKAK FVLY. |
| File.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sagl) Consensus Sun4 | Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus Sun4 |

FIG. 22(

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, et al.

EIGHT REPEATS IN UTH4

| 193 | LatDqFGcrFLQKkLE |
|-----|------------------|
| 231 | LilDpFGnyLVdKicD |
| 267 | IsingYGtrsLQKiID |
| 310 | LinDInGnhVIQKcIf |
| 348 | IstHkhGccVLQKiLs |
| 384 | LinDqFGnyIIQfiLD |
| 422 | LsclkFssnVVeKfIK |
| 487 | LirDnFGnyALQtlLD |

HYDROPHOBIC CHARGED

FIG. 23

Title: Genes Determining Cellular Senescence... Inventors: Leonard P. Guarente, *et al*.

| UTH4 YGL023 PUMILIO HUMAN | LatDqFGCRFLQKkLE LckDqHGCRFLQKqLD FsqDqHGSRFIQQkLE FsqDqHGSRFIQLkLE | i |
|------------------------------------|--|---|
| | Lil DpFGNYLIQKiCD Lmt DsFGNYLIQKiLE Lmt DvFGNYVIQKfFE Lmr DvFGNYVIQKfFE | 2 |
| | IsiNqYGTRSLQKiID IslNpHGTRALQKIIE LalQmYGLRVIQKaLE LalQmYGLRVIQKaLE | 3 |
| | LinDlNGNHVIQKcIF LskDlNGNHVIQKcLQ CvkDqNGNHVVQKcIE CvkDqNGNHVVQKcIE | 4 |
| | IstHkHGCCVLQKILS IatHrHGCCVLQRcLD LstHpYGCRVIQRiLE LstHpYGCRVIQRiLE | 5 |
| | Lin DqFGNYIIQFiLD Ltl DpFGNYVVQYiIT Liq DqYGNYVIQHvLE Lvq DqYGNYVIQHvLE | 6 |

LscIkFSSNVVEKfIK
LsiHkFGSNVIEKiIK
TSqHkFASNVVEKcVT
VlsQhFASNVVEKcVT

Lir DnFGNYALQT1LD LlnDsyGNYVLQTaLD MmkDqYANYVVQKmID MmkDqYANYVVQKmID

FIG. 24